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10/564,861	01/12/2006	Dmitry Dmitrievich Genkin	06-1664	4117
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EXAMINER BRADLEY, CHRISTINA				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/564,861

Applicant(s)

GENKIN ET AL.

Examiner

Christina Marchetti Bradley

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SG/US)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

1. Claims 1-14 are pending.

Priority

2. Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in Russia on 7/14/2003. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

Specification

3. The abstract of the disclosure is objected to because it is longer than 150 words. Correction is required. See MPEP § 608.01(b).

Claim Objections

4. Claims 1-14 are objected to because of the following grammatical errors: in claim 1, the use of the phrase "introducing of", and the lack of article before "blood extracellular DNA destroying agent"; in claim 2, the use of the phrase "which characterized by", the use of the phrase "introducing of" and the lack of article before "blood extracellular DNA electrophoretic profile"; in claim 3, the space after "activity"; in claim 6, the use of the verb "it is", the space after "it is", the lack of commas in the numbers 50 000 and 250 000 000; in claim 8, the use of the verb "it is"; in claim 11, the space after "anti-"; in claim 12, the use of the word "modificating", the use of the word "polymery" and the use of "an" as the article for

“modifying”; in claim 12, the lack of comma before “which” and after “DNA”; and in claim 14, the use of the organism “*Serratia Mercenses*” which should be italicized. Appropriate correction is required.

Claim Rejections - 35 USC § 112/101

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-14 are drawn to a method for the treatment of oncological diseases, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it fails to recite any active, positive steps delimiting how the method is actually practiced. In the instant case, claim 1 states that the method is “characterized by introducing of blood extracellular DNA destroying agent”. The use of the phrase “characterized by” renders the claim indefinite because it is not clear if the limitation following this phrase is an active, method step.

7. Claims 1-14 are rejected under 35 U.S.C. 101 because the claimed recitation of a method, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 recites the limitation "introducing of blood extracellular DNA destroying agent". There is more than one interpretation for this limitation. The limitation could be interpreted as "introducing of blood", that is the administration of blood. Alternatively, the word blood could be read as modifying extracellular DNA, implying administering an agent that destroys extracellular DNA found in blood.

11. Claim 1 recites the limitation "blood extracellular DNA destroying agent". The term "destroying agent" is not defined in the specification. The specification also fails to define destroyed DNA. Several interpretations exist including hydrolysis of DNA to smaller fragments, hydrolysis of DNA to nucleotides, and a breakdown of the molecule to carbon, nitrogen, hydrogen, oxygen and phosphorous. In addition, the agent could act indirectly on the DNA, reducing its presence in blood by inhibiting its production.

12. Claim 1 recites the limitation "the treatment". There is insufficient antecedent basis for this limitation in the claim.

13. Claim 2 recites the limitation "which characterized by". The lack of verb in this claim renders the claim indefinite for omitting steps.

14. Claim 6 recites the limitation "wherein bovine pancreatic DNase is used". It is not clear if the bovine pancreatic DNase is being used as the blood extracellular DNA destroying agent or

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for some other purpose. As a result, the claim omits essential steps on how to use the bovine pancreatic DNase.

15. Claim 7 recites the limitation "wherein human recombinant DNase is used". It is not clear if the human recombinant DNase is being used as the blood extracellular DNA destroying agent or for some other purpose. As a result, the claim omits essential steps on how to use the bovine pancreatic DNase.

16. Claim 9 recites the limitation "the treatment is carried out for term of life". There is insufficient antecedent basis for "term of life" because no subject is recited in claim 1.

17. Claim 10 recites the limitation "wherein in addition to the said treatment an agent binding extracellular DNA is introduced". The claim omits the essential element of the subject. In addition, it is unclear if this limitation is part of the treatment method or if it severs another purpose.

18. Claim 12 recites the word "polymer" which is not defined in the specification or commonly used in the protein and nucleic acid art.

19. Claim 13 recites the limitation "said agent". There is insufficient antecedent basis for this limitation in the claim. The agent could be the modifying agent of claim 12 or the blood extracellular DNA destroying agent of claim 1.

20. Claim 14 recites the limitation "said agent". There is insufficient antecedent basis for this limitation in the claim. The agent could be the modifying agent of claim 12 or the blood extracellular DNA destroying agent of claim 1.

21. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP

§ 2172.01. The omitted elements are: the identification of the "systemic blood circulation". This term could be interpreted as the blood of a patient or any circulating blood system. The claim likewise omits the identification of the subjects of the method.

Claim Rejections - 35 USC § 112

22. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating Erlich carcinoma in mice, lung carcinoma in humans and malignant, low differentiated lymphoma metastasized in the liver of humans by administering DNase to patients, and for treating Erlich carcinoma in mice by administering DNase and anti-DNA antibodies, does not reasonably provide enablement for treating all other oncological diseases with DNase or any other DNA destroying agent with or without the addition of "modifying agents" or other DNA binding agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and are as follows:

The Nature of the Invention

24. The invention is drawn to a method for treating oncological diseases by administering a blood extracellular DNA destroying agent.

The State of the Prior Art and its Predictability or Unpredictability

25. Anker *et al.* (*Leukemia*, **2001**, *15*, 289-91 teach that circulating DNA levels are higher in the blood of cancer patients than in healthy controls (page 289). The prior art does not teach or suggest that cancer can be treated by reducing the circulating DNA levels.

The Relative Skill of Those in the Art

26. The relative skill of those in the art is high.

The breadth of the claims

27. The claims are exceptionally broad with respect to both the compounds and their intended use. A blood extracellular DNA destroying agent can include an agent that directly or indirectly acts to reduce the level of extracellular DNA circulating in blood. Said agent may hydrolyze the DNA into smaller fragments or nucleotides, or degrade the DNA to its elemental state. The intended use of these compounds is likewise broad because oncological diseases include all types of cancer known to affect humans and animals.

The Amount of Direction or Guidance Presented and the Presence of Working Examples

28. The specification presents only one working example of a blood extracellular DNA destroying agent, deoxyribonuclease (DNase). This enzyme may be bovine pancreatic DNase, human recombinant DNase or other forms of DNase known in the art. The specification fails to define blood extracellular DNA destroying agent and to provide guidance on how to isolate other agents with the claimed ability to destroy blood extracellular DNA.

29. The specification presents working examples of the treatment of three oncological diseases: Erlich carcinoma in mice (examples 1 and 2), lung carcinoma in humans (example 3) and malignant, low differentiated lymphoma metastasized in the liver of humans (example 4). In

each case, the administration of DNase resulted in a reduction in circulating extracellular DNA and tumor. The specification fails to provide working examples for the treatment of any additional oncological diseases.

30. The specification presents only one working example of an “agent binding the blood extracellular DNA”, polyclonal serum containing anti-DNA antibodies (example 6). The specification fails to define agent binding the blood extracellular DNA”, and to provide guidance on how to isolate other agents with the claimed ability to bind extracellular DNA.

31. The specification fails to present a single working example involving the administration of a “modifying agent”. Example 7 describes the effect of “modifying agents” on the pathogenic properties of DNA that has been extracted from plasma, and then subsequently administered to patients, but does not describe the effect of directly administering the “modifying agent”.

The Quantity of Experimentation Necessary

32. The extent of guidance and working examples presented in the specification is insufficient to enable the full scope of the claimed methods. The skilled artisan would be burdened with testing all agents known to have a destructive effect on DNA for their ability to treat a wide range of oncological diseases. The skilled artisan would be further burdened with testing the administration of DNA destroying agents in combination with DNA binding and “modifying” agents. The experimentation required represents years of inventive effort. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

34. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Ngan *et al.* (*Ann. NY Acad. Sci.*, **2001**, 945, 73-79). Ngan *et al.* teach the administration of cisplatin to patients suffering from nasopharyngeal cancer (page 74). The administration of cisplatin resulted in a reduction of free Epstein-Barr virus DNA circulating in the patient's plasma and complete or partial remission in 76% of the patients (page 75). Thus, the cisplatin was administered in an amount sufficient to destroy blood extracellular DNA in these patients and to treat the oncological disease.

Double Patenting

35. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

36. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

37. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

38. Claims 1-3 and 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/564,609 in view of Anker *et al.* (*Leukemia*, **2001**, *15*, 289-91). Claim 1 of copending Application No. 10/564,609 recites a method for treating diseases associated with changes of blood extracellular DNA by introducing an extracellular DNA destroying agent. Dependent claims 2-4 recite DNase as the DNA destroying agent. The claims do not recite a method for treating oncological diseases specifically although they recite “diseases caused by mutations in somatic cell’s genes” as part of the genus of diseases that can be treated by the claimed method. Anker *et al.* teach that circulating DNA levels are higher in cancer patients than in healthy controls (page 289). It would have been obvious to apply the method of treatment recited in claim 1 of copending Application No. 10/564,609 to cancer patients. The skilled artisan would have been motivated to do so based on the fact that the claimed method is intended to treat diseases characterized by a change in blood extracellular DNA, as evidenced by the preamble, and the fact that cancer is characterized by increases in circulating DNA, as evidenced by the teaching of Anker *et al.* This is a provisional obviousness-type double patenting rejection.
39. Claims 1-3 and 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 13 of copending Application No. 10/546,615. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 of copending Application No. 10/546,615 recites a method for treating oncological, infectious or somatic diseases by targeting extracellular DNA circulating in blood plasma. Claim 13 of copending Application No. 10/546,615 recites DNase as an agent for targeting extracellular DNA circulating in blood plasma. There is no claim to the species

oncological disease nor does the claim specifically recite the administration of the DNase as part of the treatment method. Anker *et al.* teach that circulating DNA levels are higher in cancer patients than in healthy controls (page 289). It would have been obvious to apply the method of treatment recited in claim 1 of copending Application No. 10/546,615 to patients with oncological diseases. The skilled artisan would have been motivated to do so based on the fact that the claimed method is intended to target blood extracellular DNA, as evidenced by claim 1, and the fact that cancer is characterized by increases in circulating DNA, as evidenced by the teaching of Anker *et al.* It would have been further obvious to administer DNase as part of this treatment method based on the fact that claim 13 states that DNase is pharmaceutical agent for oncological disease that can target circulating DNA. This is a provisional obviousness-type double patenting rejection.

Conclusion

40. No claims are allowed.
41. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 8:30 A.M. to 3:30 P.M.
42. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
43. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Christina Marchetti Bradley/
Examiner, Art Unit 1654

